IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

IN RE: AVANDIA MARKETING, SALES PRACTICES AND PRODUCT LIABILITY LITIGATION	CIVIL ACTION NO. MDL No. 1871 2:07-md-01871-CMR Hon. Cynthia M. Rufe
THIS DOCUMENT RELATES TO Case No.: 2:10-CV-01637-CMR	
COUNTY OF SANTA CLARA and THE PEOPLE OF THE STATE OF CALIFORNIA, acting by and through Acting Santa Clara County Counsel Lori E. Pegg, Plaintiffs, vs. SMITHKLINE BEECHAM CORPORATION d/b/a GLAXOSMITHKLINE L.L.C., Defendant.	

SECOND AMENDED COMPLAINT FOR DAMAGES AND DEMAND FOR JURY TRIAL

INTRODUCTION

1. In the mid 1990s, Defendant GlaxoSmithKline ("GSK") began testing rosiglitazone maleate, a newly-developed diabetes medication commonly known as Avandia, for which GSK was seeking FDA approval. These early studies and others conducted in the wake of FDA approval revealed that Avandia significantly ***increased*** the risk of heart attack and death for patients with diabetes. GSK ignored or concealed these findings and instead engaged in an aggressive and highly successful marketing strategy designed to replace equally effective, less expensive, and far safer diabetes drugs already on the market. GSK's aggressive marketing strategy, combined with its successful cover-up of mounting evidence regarding the increased cardiovascular risks associated with Avandia, resulted in billions of dollars in profits for GSK and an estimated 60,000 to 200,000 excess heart attacks, strokes, and other cardiovascular deaths between 1999 and 2006.

2. In 2007, after GSK had been concealing or down-playing substantial evidence regarding the risks of Avandia for more than a decade, the risks associated with Avandia finally became public. In an article published in the *New England Journal of Medicine* ("*NEJM*"), researchers published the results of a study through which they determined that diabetics taking Avandia were 43% more likely to suffer a heart attack, and 64% more likely to die from cardiovascular causes than similar patients taking a different diabetes medication. On July 30, 2007, the Endocrinologic and Metabolic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee of the United States Food and Drug Administration ("FDA") met in a special joint session to discuss the cardiovascular risks posed by the diabetes drug rosiglitazone maleate, commonly known as Avandia. The proceedings' chairman, Clifford M. Rosen, M.D., wrote in the August 9, 2007 edition of the "*NEJM*" that:

> The basic plot of the [Avandia] story quickly became obvious to the advisory committee: a new "wonder drug," approved prematurely and for the wrong reasons by a weakened and underfunded government agency subjected to pressure from industry, had caused undue harm to patients.

These two FDA committees officially concluded that Avandia posed greater cardiovascular risks than placebo. This increased risk is particularly troubling because diabetics already suffer from an increased risk for such events as compared to non-diabetics, and a central purpose of diabetes management through medication is to reduce that risk.

3. GSK manufactured Avandia and marketed it as a "wonder drug." From its launch in 1999 to the present, when independent medical studies have made public Avandia's true cardiac risks, GSK successfully executed a massive, aggressive marketing campaign designed to obfuscate these risks, asserting that Avandia was a "significant advance" in diabetes treatment. GSK affirmatively represented that Avandia was superior to existing drugs, such as metformin and sulfonylureas, at lowering diabetics' blood sugar, a critical goal in diabetes treatment. And GSK did not just fail to disclose the potential cardiovascular risks Avandia posed, which include heart attacks and sudden cardiac death. It affirmatively represented that Avandia could ***reduce*** diabetics' cardiovascular risks. GSK knew or should have known that these representations were not true and were likely to deceive. There simply was no scientific support for them. GSK knew or should have known even before the launch that Avandia was no better at lowering blood sugar than existing medications, and that it posed serious increased cardiovascular risks. Indeed, not only did GSK know it had no data to support its claims of CV risk and glucose reduction superiority when it made those claims, but, on information and belief, it actively manufactured data through company-sponsored "clinical trials" and "studies" that were designed solely to support GSK's marketing messages. And, upon information and belief, if there was no way to contort the "data" yielded by those trials and studies to fit the marketing message, it was company policy to bury both the data and the analysis and not release it to the public.

4. GSK's marketing strategy was wildly successful. Through 2007, GSK's U.S. Avandia sales topped $7 billion. But as Avandia revenue streamed into GSK, information began to come to light that belied GSK's claims of Avandia's superiority over the older and cheaper diabetes drugs and of its purported ability to reduce diabetics' cardiovascular risks. Indeed, GSK, through its own internal studies and reports from the field (called serious adverse event reports, or "SAEs"), collected reams of data showing that Avandia dramatically ***increased*** diabetics' cardiovascular risks. But rather than informing the public about these dangers, GSK suppressed the data and studies for fear they would undermine the drug's core marketing messages.

5. GSK knew that the dissemination of information about Avandia's true cardiovascular risks would devastate its efforts to promote the drug. When doctors outside of GSK raised suspicion about Avandia's safety, GSK set out to intimidate and silence them. Such was the official finding of the United States Senate's Finance Committee, which conducted an investigation into GSK's attempts to keep a leading diabetes expert, Dr. John Buse, from voicing his concerns about Avandia. The Committee concluded that GSK had executed "an orchestrated plan to stifle the opinion" of Dr. Buse, and that the intimidation scheme involved "executives at the highest level of GSK, including then and current CEO Jean-Pierre Garnier."

6. Ultimately, GSK could successfully conceal and misrepresent Avandia's risks for only so long. In 2007, four independent, peer-reviewed medical research studies were published showing that Avandia increased diabetics' preexisting cardiovascular risks. The most prominent study appeared in the June 14, 2007 edition of the *NEJM*. This study concluded that Avandia "was associated with a significant increase in the incidence of myocardial infarction [heart attack] and with an increase in the risk of death from cardiovascular causes . . . ." This and the

FDA's own study led the FDA to require a "black box warning" on Avandia's product label to inform consumers of such risks beginning on November 14, 2007.

7. Further, a study published in the *Annals of Internal Medicine* in September of 2007 concluded that when compared "with newer, more expensive agents [like Avandia], older agents (second-generation sulfonylureas and metformin) have similar or superior effects on glycemic [blood sugar] control, lipids, and other intermediate endpoints." Another study conducted by researchers at Harvard University and published in February 2010 in the journal of the American Diabetes Association, *Diabetes Care*, found that Avandia increases a diabetic's heart attack risk by ***30%*** compared with the older diabetes drug sulfonylurea. And when compared with metformin, Avandia increases a diabetics' heart attack risk by ***120%***.

8. Avandia's sales and distribution have suffered dramatically from these disclosures. Avandia sales are off 70% from the peak in 2007. Numerous organizations, including the American Diabetes Association and its European counterpart have dropped Avandia from their recommended drugs lists. Health insurers like Kaiser Permanente and government agencies like the Veteran's Administration have dropped Avandia from their formularies. In September 2009, the COUNTY OF SANTA CLARA also dropped Avandia from its formulary. The FDA has announced it will hold a public meeting in July 2010 on Avandia's cardiac risks.

9. In February 2010, the United States Senate Finance Committee released a report concluding, among other things, that:

> The totality of evidence suggests that GSK was aware of the possible cardiac risks associated with Avandia years before such evidence became public. Based on this knowledge, GSK had a duty to sufficiently warn patients and the FDA of its concerns in a timely manner. Instead, GSK executives intimidated independent physicians, [and] focused on strategies to minimize findings that Avandia may increase cardiovascular risk . . . .

Rather than issue proper warnings and provide accurate information about Avandia's risks and benefits, GSK chose instead to keep its deceptive propaganda and marketing machine running full steam and never took any affirmative steps to correct the misinformation and deceptive advertising scheme that it had and continued to perpetrate, ensuring that it would continue to maximize the prescription and sale of Avandia so long as diabetics, physicians, and the general public remained unaware of Avandia's true risks.

10. In addition to the resulting personal injuries, unnecessary deaths, and the profound implications for public health, the financial toll that GSK's false and deceptive marketing of Avandia has had on purchasers—including California purchasers—has been dramatic. Relying upon GSK's promises of superior treatment and better cardiovascular outcomes compared with the older diabetes drugs, Avandia purchasers paid a hefty premium. Data obtained by the Mayo Clinic showed that in October 2007 the average monthly prescription cost for older diabetes drugs like metformin varied from $4 to $100. The cost for Avandia varied from $90 to $220. No justification exists for such a premium.

11. These costs are of special significance to the State of California, which has the largest number of diabetics in the United States. Over 3 million people in California suffer from diabetes. And GSK specifically targeted its Avandia marketing scheme to California diabetics—a population California law recognizes as among the disabled—and to California senior citizens.

12. GSK's false, misleading and deceptive marketing of Avandia resulted in hundreds of millions of dollars of Avandia sales to California residents, sales that otherwise would not have been made. GSK profited from its suppression of the truth and misleading promotion of Avandia, costing California patients, their insurers, public health care providers, and government

payors large sums of money at a time when healthcare costs already were spiraling higher. The COUNTY OF SANTA CLARA alone spent nearly $2 million on Avandia.

13. GSK's false, misleading and deceptive marketing of Avandia also resulted in those California residents who took it experiencing cardiovascular side effects including, but not limited to, heart attacks, strokes, and sudden cardiac death, requiring otherwise avoidable hospitalizations and medical care and treatment. As a result, California Avandia users, their insurers, public health care providers, and government payors—i.e., the COUNTY OF SANTA CLARA—bore additional costs for the care and treatment of these undisclosed increased cardiovascular risks.

14. To protect the public from Defendants' false, deceptive and/or misleading advertising practices, Plaintiffs COUNTY OF SANTA CLARA and the PEOPLE OF THE STATE OF CALIFORNIA (the "PEOPLE"), acting by and through Acting Santa Clara County Counsel Lori E. Pegg (collectively, "Plaintiffs"), bring this suit for the benefit of certain California diabetics who purchased Avandia and other entities that purchased Avandia in California. The claims of the PEOPLE OF THE STATE OF CALIFORNIA, however, have been released, except to the extent permitted by Paragraph 11(E) of a Final Judgment entered in *People of the State of California v. GlaxoSmithKline LLC* on November 15, 2012 in the Superior Court of San Diego County. This action, therefore, asserts only the claims expressly not released in Paragraph 11(E) of the Final Judgment. To the extent permitted by Paragraph 11(E), this action seeks restitution of all money wrongfully acquired by defendants from the sale of Avandia and restitution for hospital and medical care and treatment provided to Avandia users who suffered heart attacks, strokes, and/or sudden cardiac death, whether expended by California Avandia users, their insurers, public health care providers, or government payors, including the COUNTY OF SANTA CLARA, on or after May 25, 1999, through the present. To the extent

permitted by Paragraph 11(E), Plaintiffs also seek civil penalties and all other relief to which it and the PEOPLE are entitled.

I. PARTIES

15. The COUNTY OF SANTA CLARA operates and manages the Santa Clara Valley Health & Hospital System (SCVHHS), which provides integrated hospital, clinic-based, pharmaceutical, and preventive medical services to a large indigent population. Subject to the provisions of paragraphs 89 and 90 below, the COUNTY OF SANTA CLARA and the PEOPLE OF THE STATE OF CALIFORNIA, acting by and through Acting Santa Clara County Counsel Lori E. Pegg, bring this action pursuant to California *Business and Professions Code* sections 17500 *et seq.*, and California *Civil Code* section 3345. Plaintiffs seek recovery of money wrongfully acquired by Defendants as a result of their false and deceptive marketing and sale of the diabetes drug rosiglitazone, which was advertised, marketed, and sold under the trade names Avandia® Tablets, Avandamet® Tablets, and Avandaryl® Tablets ("Avandia"), and restitution of all money for hospital and medical care and treatment provided to Avandia users who suffered heart attacks, strokes, and/or sudden cardiac death, whether expended by California Avandia users, their insurers, public health care providers, or government payors including the COUNTY OF SANTA CLARA, on or after May 25, 1999, through the present within the State of California.

16. Defendant SmithKline Beecham Corporation d/b/a GlaxoSmithKline is a Pennsylvania Corporation, with its principal place of business located at One Franklin Plaza, 200 North 16th Street, Philadelphia, Pennsylvania. SmithKline Beecham Corporation d/b/a GlaxoSmithKline is a wholly owned subsidiary of GlaxoSmithKline, PLC, and also conducts pharmaceutical research and development in the United States under the corporate fictitious name GlaxoSmithKline. Plaintiff is informed and believes, and upon such information and

belief alleges, that at all relevant times SmithKline Beecham Corporation d/b/a GlaxoSmithKline manufactured, advertised, labeled, marketed, promoted, sold, and distributed rosiglitazone in the United States, including the State of California.

17. Defendant GlaxoSmithKline, PLC, is a British corporation headquartered at Glaxo Wellcome House, Berkley Avenue, Greenford, Middlesex, England. GlaxoSmithKline, PLC, has its principal place of business in the United States at One Franklin Plaza, 200 North 16th Street, Philadelphia, Pennsylvania. In December 2000, GlaxoSmithKline, PLC, acquired Glaxo Wellcome, PLC, and SmithKline Beecham, PLC, both British public limited companies. At all relevant times, GlaxoSmithKline, PLC, was the holding company of SmithKline Beecham Corporation d/b/a GlaxoSmithKline, which was engaged in the business of marketing and/or distributing Avandia throughout the United States, including in the State of California, and it derives substantial revenues from goods purchased and consumed in California.

18. Plaintiffs are informed and believe, and upon such information and belief allege, that in committing the acts alleged herein, each and every managing agent, agent, representative, joint venturer, and/or employee of Defendants was working within the course and scope of said agency, representation, joint venture, and/or employment with the knowledge, consent, ratification, and authorization of all of the other Defendants and their directors, officers, and/or managing agents.

19. At all relevant times, Defendants packaged, distributed, supplied, sold, placed into the stream of commerce, labeled, described, marketed, advertised, promoted, and purported to warn or to inform users regarding the risks associated with the use of the prescription pharmaceutical drug Avandia.

20. The true names and capacities, whether individual, corporate, associate, or otherwise, of Defendants named herein as DOES 1 through 100, and each of them, are unknown to Plaintiff, who therefore sues said Defendants by such fictitious names. Plaintiff shall seek leave to amend this Complaint to state said Defendants' true identities and capacities when the same have been ascertained. Plaintiff is informed and believes, and based thereupon alleges, that each of the Defendants designated herein as DOE took part in and participated with, and/or aided and abetted, all of the other Defendants in all matters referred to herein and was in some manner responsible for the losses suffered by California Avandia users, their insurers, public health care providers, or government payors, including Plaintiff COUNTY OF SANTA CLARA.

21. Plaintiffs are informed and believe, and based upon such information and belief allege, that at all relevant times, each Defendant occupied agency, employment, joint venture, or other relationships with each of the other named and DOE Defendants; and that at all times herein mentioned each Defendant acted within the course and scope of said agency, employment, joint venture, and/or other relationship; and that each other Defendant has ratified, consented to, and approved the acts of its agents, employees, joint venturers, and representatives; and that each actively participated in, aided and abetted, or assisted one another in the commission of the wrongdoing alleged in this Complaint.

22. At all relevant times Defendants, and each of them, were engaged in the business of, or were successors in interest to, entities engaged in the business of researching, licensing, designing, formulating, compounding, testing, manufacturing, producing, processing, assembling, inspecting, distributing, marketing, labeling, promoting, packaging, advertising, distributing, and/or selling the prescription drug products Avandia, Avandamet and Avandaryl as

antidiabetic medications to California Avandia users, their insurers, public health care providers, or government payors, including Plaintiff COUNTY OF SANTA CLARA.

23. At all relevant times Defendants were authorized to do business within the State of California and did in fact sell and supply Avandia to individuals and entities located within the State of California.

II. JURISDICTION AND VENUE

24. The Court has jurisdiction over this lawsuit under 28 U.S.C. § 1332(a)(1) because Plaintiffs and Defendants are citizens of different states and the amount in controversy exceeds $75,000, excluding interest and costs.

25. At all relevant times, Defendants transacted business and violated California law by (1) making false and misleading statements or representations regarding the efficacy and safety of the prescription drug Avandia that were likely to deceive and did deceive diabetics, medical professionals, and the general public; (2) making such statements in connection with the marketing, promoting, distributing, and/or selling of Avandia in interstate commerce and in the State of California; (3) failing to disclose material facts regarding the efficacy and safety of the prescription drug Avandia, which in the absence of such disclosures was likely to deceive and did deceive the general public; (4) failing to make such disclosures in connection with the marketing, promoting, distributing, and/or selling of Avandia in interstate commerce and in the State of California; and (5) engaging in this conduct in the regular course of Defendants' trade or commerce.

26. At all relevant times, Defendants purposefully availed themselves of the benefits and protections of the laws of the State of California.

27. Defendant GSK had and still has sufficient contacts within the State of California that the exercise of jurisdiction is consistent with the traditional notions of fair play and substantial justice.

28. This case was originally filed in the United States District Court for the Northern District of California, where venue is proper under 28 U.S.C. Section 1391(a)(2). The case was transferred to the Eastern District of Pennsylvania as part of a multidistrict litigation proceeding under 28 U.S.C. Section 1407, and Plaintiff will seek remand of the case to its court of original filing.

III. FACTS SURROUNDING DEFENDANTS' DECEPTIVE MARKETING

A. The Basic Medicine of Diabetes.

29. Type 2 diabetes, the most common form of diabetes, results from the body's failure to produce enough insulin (insulin deficiency) and/or inability to use insulin properly (insulin resistance). Insulin is necessary to process and remove blood sugar. Without insulin, sugar builds up in the bloodstream and cells are starved for energy. This can cause tissue breakdown, which can lead to numerous health dangers, such as kidney failure, blindness, and amputations. Furthermore, diabetics are at an increased risk, as compared to non-diabetics, for atherosclerosis, heart attacks, strokes, kidney disease, and nervous system damage. Thus, drugs designed to treat diabetes must be sensitive to, among other things, diabetics' preexisting cardiovascular risks.

30. The "first line" of treatment for Type 2 diabetes consists of established and inexpensive oral medications, primarily sulfonylureas and metformin. Indeed, metformin is recognized as the "gold standard" in Type 2 diabetes treatment. In its "Standards of Medical Care in Diabetes 2009," the American Diabetes Association noted that the consensus for treating

Type 2 diabetes begins with "intervention at the time of diagnosis with metformin in combination with lifestyle changes and continuing timely augmentation of therapy with additional agents (including early initiation of insulin therapy) as a means of achieving and maintaining recommended levels of glycemic control." Metformin reduces the amount of sugar released by the liver between meals, promotes weight loss, and reduces cholesterol and triglycerides levels. Its side effects are minimal and include nausea and upset stomach. Sulfonylureas stimulate the pancreas to produce more insulin. Sulfonylureas combine well with other diabetes drugs for maximum effect on blood sugar; their side effects include hypoglycemia (low blood sugar) and weight gain. As a diabetic's disease progresses, medications may be added to the patient's regimen, including the use of insulin.

B. Diabetes is a Major Health Problem in California.

31. Diabetes affects more than 17 million people nationwide. It disproportionately affects the elderly; approximately 20% to 25% of seniors have diabetes. Recently, Type 2 diabetes has increased sharply in children and adolescents, a development that is intertwined with the growing obesity problem in the United States.

32. In California in particular, diabetes is a major public health problem. There are three million diabetics currently residing in California, with that number expected to ***double*** by the year 2020. Diabetes disproportionately impacts California's low income individuals and families, minorities, and senior citizens. According to the U.S. Centers for Disease Control and Prevention's Behavioral Risk Factor Surveillance System, in 2008 diabetes afflicted 14.7% of Californians with an annual income under $15,000—more than 1 in every 7 individuals. Also in 2008, while 6.9% of white Californians had diabetes, the rates were substantially higher among people of color: 9.7% of Latino Californians and 15.7% of African-American Californians

suffered from the disease. And a full 20.1% of Californians aged 65 and older had been diagnosed with diabetes—1 in every 5 seniors. Those numbers continue to rise.

33. As the diabetes problem grows in California, public entities, public health care providers, public hospitals, and government payors, such as the COUNTY OF SANTA CLARA, have had to shoulder an increasing share of the burden of treating diabetics, particularly in indigent and low-income populations; the weight of that responsibility continues to grow. Public entities, public health care providers, public hospitals, and government payors seek the most effective and safest treatment for their patients and rely on pharmaceutical companies to fairly and accurately represent the safety and efficacy of their products. As previously indicated, Plaintiff COUNTY OF SANTA CLARA operates and manages the Santa Clara Valley Health & Hospital System (SCVHHS), which provides integrated hospital, clinic-based, pharmaceutical, and preventive medical services to a large indigent population. To treat patients with Type 2 diabetes, SCVHHS purchased approximately $2 million worth of Avandia starting in 1999, relying on GSK's false and misleading representations that Avandia was a safe and effective treatment for Type 2 diabetes. GSK's deception increased the costs to public entities, public health care providers, public hospitals, and government payors, including SCVHHS, through the higher price of Avandia when cheaper and safer alternatives were available. Further, public entities, public health care providers, public hospitals, and government payors such as Plaintiff COUNTY OF SANTA CLARA bear the additional treatment and hospitalization costs of the heart attacks and other cardiovascular problems caused by Avandia to its users including, but not limited to, heart attacks, strokes, and sudden cardiac death. GSK could have prevented these increased costs had it been forthcoming with the medical and scientific community and consumers about the risks of Avandia.

C. Avandia's Pre-Launch Years: 1996-1998.

34. Avandia is one of a newer generation of diabetes drugs called thiazolidinediones ("TZDs"). These drugs lower blood sugar like the established "first-line" drugs.[1] Avandia and other TZDs do this by allegedly sensitizing the body to use insulin more efficiently and effectively. Years before Avandia hit the market, however, GSK[2] was aware of Avandia's potential to cause serious cardiovascular problems.

35. In preparation for seeking the FDA's approval to put the drug on the market, GSK conducted five clinical studies between 1996 and 1998 that revealed a high number of deaths among patients treated with Avandia. Eight Avandia patients suffered heart attacks or cardiac deaths, as compared to only three in the control group. This data alone should have alerted GSK to Avandia's increased cardiovascular risk. Nevertheless, GSK failed to act on this data and continued its plan to seek FDA approval for Avandia.

36. On November 25, 1998, in spite of its knowledge of the drug's increased cardiovascular risks, GSK submitted Avandia's New Drug Application ("NDA") to the FDA.

D. GSK Launches Its "Significant Advance" in Diabetes Treatment: 1999.

37. Beginning in early 1999, while Avandia's New Drug Application was under consideration by the FDA, GSK's false and deceptive Avandia marketing campaign took form. GSK's targeted competitor drugs were not only other TZDs. Rather, GSK sought to achieve

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[1] The safety and efficacy of TZD drugs in general is questionable, as at least two TZDs have been either removed from the market or never approved by the FDA due to their health risks. Troglitazone, known as Rezulin, was removed from the market due to its high risk of liver damage. The FDA did not approve another TZD, muraglitazar, a drug similar to Avandia, because of its demonstrated cardiovascular risks.

[2] SmithKline Beecham owned Avandia before January 18, 2000. On January 18, 2000, SmithKline Beecham merged with the British company Glaxo Wellcome, forming Defendant GlaxoSmithKline, or GSK.

dominance in the Type 2 diabetes market by becoming the preeminent "first-line" drug of choice. It sought to replace not only other TZDs but also metformin and sulfonylureas—the established, ***much*** safer, and ***much*** cheaper diabetes drugs.

38. GSK spent hundreds of millions of dollars in a far-reaching, massive, and widespread promotional campaign to drive Avandia's sales. A highly sophisticated marketer of pharmaceutical products, GSK used its substantial sales, marketing, and public relations machines to create a false and misleading impression of the drug's safety and efficacy among consumers, physicians, insurers, public health care providers, public entities, and government payors including Plaintiff COUNTY OF SANTA CLARA.

39. Since 1999 GSK has spent millions on Direct-to-Consumer ("DTC") print and television advertising, aimed at convincing patients to request Avandia from their doctors. GSK's marketing campaign also targeted doctors as well as the individuals and groups responsible for selecting the drugs covered by health coverage plans and included on pharmacy formularies. GSK sought to influence these targets through, among other tactics, print media, misleading promotional materials, lavish company-sponsored dinners, and "conferences" at posh resorts. GSK produced and distributed "studies" whose sole purpose was to advance the company's marketing message and which were intended to, and did, deceive diabetics, medical professionals, and the general public.

40. GSK's Avandia message had two key components. First, GSK propagated the message that Avandia was better at lowering blood sugar than other established drugs. That is, Avandia had superior efficacy. GSK also represented that patients could stay on Avandia longer than the older drugs. Second, GSK represented that, unlike the older diabetes drugs, Avandia had the additional benefit of actually ***lowering*** diabetics' cardiovascular risks. The notion that

Avandia would actually lower diabetics' cardiovascular risk was critical to Avandia's marketing. GSK needed justification for the steep price difference between Avandia and the older established diabetes drugs. GSK, however, knew or should have known that these representations were false, misleading, and likely to deceive. At best, GSK had no data to support these claims. At worst, they were wholesale fabrications.

41. Indeed, upon information and belief, GSK has at all relevant times *known* that it lacked the scientific data to support its efficacy and safety claims. Instead, upon information and belief, GSK's marketing department planned to create scientific evidence to substantiate GSK's marketing claims by conducting company-sponsored "clinical trials" and "studies." On information and belief, company scientists lack the necessary independence in GSK's corporate structure to allow them to create scientific studies that meaningfully assess efficacy and safety; instead, they take direction from GSK's marketing department. On information and belief, GSK's marketing department routinely communicates with GSK scientists, directing them to design studies and trials to yield results that further the drug's product message. Thus, GSK scientists played a central role in GSK's marketing strategy by designing clinical trials and meta-analyses not to advance scientific inquiry into the drug's safety and efficacy, but to produce results consistent with (and hide results inconsistent with) GSK's preexisting advertising messages about Avandia.

42. Another central aspect of GSK's advertising campaign was restricting access to scientific data about Avandia that would support independent and critical assessments of the drug's safety. On information and belief, when GSK's scientists were unable to obtain the results for Avandia studies that the marketing department ordered, it was company policy to bury the unfavorable data either by not releasing it at all, or by obscuring the data's import by

releasing only "summary findings" on the company's website, making the data impossible for independent scientists to analyze effectively.[3]

43. Another vehicle of GSK's tight message construction and control was its use of sales representatives who spread the Avandia message by calling on thousands of physicians throughout the State of California. GSK even used seemingly independent physicians to disseminate its message. On information and belief, GSK paid doctors to act as speakers to deliver the company's messages about the drug at conferences and in other professional venues, and as writers who collaborated with GSK representatives in the "ghostwriting" of medical and scientific articles that sought to advance GSK's Avandia marketing agenda. "Ghostwriting" is a particularly insidious practice where a drug company authors a purportedly independent scientific paper and then pays someone else to place ***their*** name on the paper to give the appearance of independence and objectivity by suggesting that the independent person or group, and ***not*** the drug company, performed the research and authored the paper. This aspect of GSK's messaging campaign was particularly far-reaching and effective, as revealed by an independent study authored by doctors at the Mayo Clinic and published in the March 19, 2010 *British Medical Journal* ("BMJ"). The study surveyed 202 articles written about Avandia. The BMJ study found that out of the 31 unique authors who expressed "favourable opinions" of Avandia, 27 of them—an extraordinary 87 percent—had financial ties to GSK.

[3] GSK's policy of burying unfavorable data or releasing only "summary findings" was a major complaint of the *Nissen* study's authors. They wrote in the June 14, 2007 edition of the *New England Journal* that GSK's "public disclosure of summary results for [Avandia] clinical trials is not sufficient to enable a robust assessment of cardiovascular risks. The manufacturer has all the source data for completed clinical trials and should make these data available to an external academic coordinating center for systematic analysis." Little did the *Nissen* authors know that there were volumes more data that GSK did not release in any form that would have revealed that Avandia is no better at lowering glucose than existing drugs, and that it dramatically increases diabetics' cardiovascular risks.

44. But even as early as 1998—***before*** the sale of the first dose of Avandia—GSK knew or should have known that Avandia was likely to cause heart attacks, strokes, and sudden cardiac death. Further, while GSK honed its false marketing message, independent scientists expressed their valid and well-founded concerns over Avandia's cardiovascular safety. One such scientist was John Buse, M.D., a leading diabetes researcher and scholar who served as an investigator for a study of Avandia sponsored by SmithKline Beecham (one of GSK's predecessor entities). At meetings of the Endocrine Society and the American Diabetes Association in early 1999, Dr. Buse publicly stated his concern that Avandia carried increased cardiovascular risks. GSK, well-aware of Dr. Buse's comments, was not concerned about the harm its drug could cause to patients. GSK was instead more worried that this information could harm their marketing campaign and bottom line corporate profits, and it became determined to silence Dr. Buse.

45. GSK's mendacious marketing campaign did not go unnoticed by the FDA. The FDA cited GSK for engaging in false and deceptive advertising for Avandia ***before*** the drug was even launched. The FDA cited GSK for precisely the core messages GSK contrived to promote, advertise, and market Avandia. In an April 23, 1999 press release, GSK touted Avandia as "a significant advance in the treatment of diabetes and [as] highly effective in safely and significantly lowering blood sugar." GSK elaborated that Avandia "can help the millions of people with type 2 diabetes lower their blood sugar levels and help prevent life-threatening complications." Federal regulations, however, prohibit a drug company from "represent[ing] in a promotional context that an investigational new drug is safe or effective" before receiving FDA approval. GSK did exactly that and in so doing intentionally violated federal regulations.

46. Nevertheless, on May 25, 1999, the FDA approved Avandia for sale in the United States as an anti-diabetic drug. In its approval letter, the FDA reminded GSK of its commitment to conduct a Phase IV post-marketing (*i.e.*, post-approval) study. GSK had previously attempted to avoid such a study. In a letter to the FDA dated May 5, 1999, GSK complained that "given the scope, complexity, and expense of such trials, [GSK] is not currently in a position to make any commitment about a long[-]term outcomes trial." Instead, GSK promised to conduct its previously planned ADOPT (A Diabetes Outcome Progression Trial) study. ADOPT was a 4-year study allegedly designed to assess, among other things, the long-term safety of Avandia as compared to two other anti-diabetic drugs. Not coincidentally, the other diabetic drugs GSK chose as comparators were metformin and the sulfonylurea glipizide, the "gold standard" medications that it sought to supplant with Avandia.

47. Shortly after Avandia's FDA approval, GSK took action against Dr. Buse, the scholar who had called Avandia's safety into question just prior to its launch. In a June 1999 e-mail, Dr. Tachi Yamada, GSK's head of research at the time, wrote to colleagues at the company:

> I plan to speak to Fred Sparling, [Dr. Buse's] former [department] chairman[,] as soon as possible. I think there are two courses of action. One is to sue [Dr. Buse] for knowingly defaming our product . . . the other is to launch a well planned offensive on behalf of Avandia . . . .

48. Additionally, GSK prepared and sent a letter to Dr. Buse, to be signed by him, "retracting" his statements about Avandia's increased cardiovascular risk.

49. As promised, Dr. Yamada called Dr. Sparling at the University of North Carolina. Shortly thereafter and in response to GSK's pressure, Dr. Buse wrote to Dr. Yamada, "clarifying" his position on Avandia. In his letter, Dr. Buse stated that he continued to "believe as a clinical scientist that the null hypothesis should be that [Avandia] has the potential to

increase cardiovascular events." Despite this belief, Dr. Buse stated that he had learned of "implied threats of lawsuits from my chairman [Dr. Sparling] and James Huang," who was then a product manager with GSK, and, succumbing to the threat of legal action, Dr. Buse asked GSK to "call off the dogs." Under pressure, he signed the so-called "retraction letter," which had been authored for his signature by GSK officials.

E. Evidence of Avandia's Dangers Mount: 2000-2003.

50. When the FDA first approved Avandia, it did ***not*** approve it for use in combination with insulin. As a part of GSK's attempt to expand Avandia's market reach, on February 7, 2000, GSK filed a supplemental New Drug Application ("sNDA") seeking FDA approval of Avandia for use with insulin.

51. Approximately one month later, on March 15, 2000, and notwithstanding his "retraction letter," Dr. Buse wrote to the FDA to voice his continuing concerns about Avandia's cardiovascular safety:

> I remain concerned about the safety of rosiglitazone in light of its constant negative impact on lipids documented in the FDA registration data as well as ***a worrisome trend in cardiovascular deaths and severe adverse events in the subjects exposed to rosiglitazone*** . . . . I do not believe that rosiglitazone will be proven safer than troglitazone in clinical use under current labeling of the two products.
>
> (Emphases added.)

52. On October 20, 2000, the FDA again found that GSK's promotional materials for Avandia, including print advertisements, were false and misleading in violation of federal law. The FDA admonished GSK that "your presentations that Avandia [] decreases [glucose] by 2.3% are ***misleading*** because they suggest that Avandia is more effective than has been demonstrated by substantial evidence." (Emphasis added.) The FDA further found that other materials were "***misleading*** because they fail to present risk information with a prominence and readability

reasonably comparable with the presentation of information related to the effectiveness of the drug." (Emphasis added.) And still more advertising material was found to "lack fair balance because materials present the product's indication without disclosing risks associated with Avandia." GSK's aggressive marketing scheme misrepresented the safety and efficacy of Avandia yet again and further demonstrated its constant disregard for the health of Avandia consumers and for the otherwise avoidable prescription and treatment costs incurred by California Avandia users, their insurers, public health care providers, public hospitals, public entities, and government payors, including Plaintiff COUNTY OF SANTA CLARA.

53. On February 7, 2001, the FDA medical officer reviewing GSK's insulin sNDA recommended rejecting the application based on mounting evidence of adverse cardiovascular events, such as heart attacks, linked to Avandia. That same FDA medical officer concluded that the safety information was "quite troublesome." In addition to mounting safety concerns, GSK continued to receive adverse event reports and other information that confirmed that its claims of Avandia's superior efficacy and greater safety over established diabetes drugs were false. Despite all this, GSK continued its false and deceptive campaign at full speed.

54. On June 28, 2001, the FDA cited GSK for a ***third*** time during its coordinated Avandia marketing campaign, this time for "direct-to-consumer (DTC) broadcast and print advertisements for Avandia that are ***false and misleading***." (Emphasis added.) The FDA found these advertisements to be false and misleading because they presented incomplete and deceptive information about the use of Avandia with insulin. Furthermore, the advertisements minimized the required warning information because they failed to use "consumer-friendly language and therefore [were] unlikely to be understood by consumers." The FDA further noted that GSK

continually made statements in its advertising that undercut and minimized the FDA-required bolded warnings relating to Avandia.

55. A month later, on July 17, 2001, the FDA cited GSK for a ***fourth*** time for, among other things, statements made by GSK sales representatives exaggerating and misrepresenting the efficacy and safety of Avandia. At a meeting of the American Diabetes Association and the American Association of Clinical Endocrinologists held on May 2-6, 2001, GSK sales representatives made oral statements that denied the existence of serious new cardiovascular risks associated with Avandia. Notwithstanding the fact that the use of Avandia with insulin had not been approved by the FDA, the same GSK representatives continually represented that Avandia was safe for use with a variety of other drugs, including insulin. The FDA's warning was coupled with the following statement:

> Your promotional activities that minimize serious new risks are particularly troublesome because we have previously objected, in two untitled letters, to your dissemination of promotional materials for Avandia that failed to present any risk information about Avandia. . . . Despite your assurances that such violative promotion of Avandia had ceased, your violative promotion of Avandia has continued.

56. Also in 2001, GSK initiated several secret Avandia studies, some apparently directly in response to the mounting cardiac adverse event reports. GSK violated federal law by not reporting these studies to the FDA. Of course, if GSK kept the studies secret, they would not have to reveal their results—unless those results turned out to be consistent with their marketing message. The individual violations for which the FDA cited GSK in 2000 and 2001 were not isolated incidents. Instead, they were integral components of GSK's entire coordinated marketing campaign—a campaign that was, as a whole, driven by the aim of misleading the public and the medical community about Avandia's efficacy and safety. While the FDA focused on these individual violations, GSK got away with countless other deceptions that contributed to

its overarching goal of suppressing adverse information and disseminating false or misleading positive information about Avandia.

57. On February 20, 2002, yet another FDA official recommended rejecting GSK's insulin sNDA for Avandia because of concerns about the increased risk of heart attacks. This official further recommended that GSK send a letter to doctors who prescribed Avandia, warning them about the increased risk of heart attacks.

58. Also in 2002, and in yet another violation of federal law, GSK failed to disclose to the FDA that it had initiated a study to look specifically at Avandia's cardiovascular safety: the RECORD (Rosiglitazone Evaluated for Cardiac Outcomes and Regulation of Glycaemia in Diabetes) study. Notably, GSK did not initiate the RECORD study on its own volition. It was actually ordered by the FDA's European counterpart, the European Medicines Agency (EMEA), to commence the study because of that agency's nascent concerns that Avandia posed serious cardiovascular risks.

59. On February 7, 2003, an FDA safety review of Avandia's insulin sNDA recommended that it should not be approved. In support of this recommendation, it cited an "excess of congestive heart failure and myocardial infarction."

60. Despite this and the other recommendations of its own personnel, the FDA approved GSK's insulin sNDA for Avandia on February 27, 2003. The EMEA rejected a parallel application in Europe based on the apparent increased risk of heart attacks. The EMEA further required GSK to include a specific warning on Avandia's label that it should ***not*** be used with insulin because of the increased heart attack risk. While GSK complied with the EMEA's order to warn diabetics and purchasers in Europe, it did nothing to warn diabetics in the United States. Thus, while GSK was representing to doctors, diabetics, and purchasers in the United

States, including California, that Avandia was safe for use with insulin, it was warning doctors, diabetics, and purchasers in Europe that it was not safe for precisely the same use.

F. GSK's Deception Begins to Surface: 2004-2006.

61. As serious cardiac adverse event reports continued to pour in, GSK decided that, in addition to its policy of concealing the data on Avandia's increased cardiovascular risks, it needed to prepare for offensive action to convince diabetics, the U.S. medical community, and the public that Avandia was safe. Thus, in 2004 it began marshalling, filtering, and selectively disseminating the data and studies it had been collecting regarding Avandia's cardiac risks.

62. In 2005, GSK concluded its own meta-analysis of data concerning Avandia's effect on diabetics' risk of heart attacks. Stunningly, GSK's own meta-analysis found that Avandia increased diabetics' risk of heart attacks by at least ***an additional 31%***. Yet, when GSK informed the FDA about its meta-analysis in September 2005, it minimized the significance of its own conclusions by stating merely that they "may" signal an increased risk for heart attacks in diabetics. GSK did not inform California diabetics, their insurers, public health care providers, public entities, or government payors, including Plaintiff COUNTY OF SANTA CLARA, of GSK's now undeniable knowledge of the increased cardiovascular risk associated with use of Avandia. Instead, its false and deceptive marketing campaign continued full speed ahead.

63. At around this same time in 2005, Dr. Buse again expressed his concerns about Avandia's increased cardiovascular risk—this time, privately, to Steven Nissen, M.D., chairman of the Cardiology Department at the Cleveland Clinic. Dr. Buse wrote:

> Steve: Great job on the muriglitazar article. [4] ***I did a similar analysis of the data at rosiglitazone's initial FDA approval*** based on the slides that were presented at

[4] Muriglitizar was a drug similar to Avandia that did not receive FDA approval, primarily because it was found to increase diabetics' risk of heart attacks. Dr. Nissen wrote an article analyzing the clinical trial data.

> the FDA hearings. I presented it at the Endocrine Society and A[merican] D[iabetes] A[ssociation] meetings that summer. Immediately the company's leadership contact[ed] my chairman and a short and ugly set of interchanges occurred over a period of about a week ending in my having to sign some legal document in which I agreed not to discuss this issue further in public. . . . ***I was certainly intimidated by them***. . . . Again congratulations on that very important piece of work. It makes me embarrassed to have caved in several years ago.

(Emphases added.) Dr. Nissen subsequently investigated Avandia's cardiac risk and published the peer-reviewed article most credited with leading to the FDA's imposition of a black-box warning in November 14, 2007.

64. In August of 2006, GSK finally sent to the FDA and EMEA the results of its 2005 meta-analysis showing that use of Avandia caused a 31% increase in diabetics' already elevated heart attack risk. Within two months, the EMEA ordered GSK to put the results of its meta-analysis on its warning label. Meanwhile, in the United States, GSK continued to minimize Avandia's risks to California diabetics, their insurers, public health care providers, public entities, and government payors, including Plaintiff COUNTY OF SANTA CLARA, of the risk.

65. While intentionally failing to warn of Avandia's known increased cardiovascular risks, GSK continued to tout "studies" consistent with its marketing message. On September 23, 2006, GSK published the results of its DREAM (Diabetes Reduction Assessment with Rampiril and Rosiglitazone Medication) study. The DREAM study allegedly investigated whether Avandia could prevent diabetes by examining the effect of Avandia on non-diabetics. While treatment with Avandia was associated with a lower risk of diabetes for pre-diabetic subjects as compared to a placebo, subjects taking Avandia had a higher incidence of heart attacks than the control group. Some scientists sharply criticized the DREAM study, noting that GSK appeared to be focused largely on marketing questions by focusing on a pre-disease state and not concentrating on addressing the pressing questions surrounding Avandia's increased risk of heart attacks for the population to whom the drug was actually marketed.

66. In December 2006, GSK released the results of its ADOPT (A Diabetes Outcome Progression Trial) study in the *NEJM*. As an integral part of GSK's marketing campaign, the ADOPT study compared Avandia to metformin and another drug called glipizide (also known as glyburide) to "compare" their glycemic control efficacy. GSK had promised the FDA that ADOPT would study, among other things, the long-term safety of Avandia, including cardiovascular risks. However, cardiovascular events were neither identified nor recorded in a systematic fashion in the ADOPT study. Heart failure was the only outcome it reviewed and measured. GSK ignored data about other cardiovascular events, such as congestive heart failure and non-fatal heart attacks—data that would have been valuable in assessing Avandia's cardiovascular risks. GSK knew there were many serious cardiovascular issues associated with Avandia aside from heart failure, but it failed to investigate these risks even when it had the opportunity to do so. Nonetheless, as two prominent researchers observed in an editorial in the *NEJM*, "even though misclassification and incomplete ascertainment of events effectively reduce the ability of a study to detect a difference in event rates, [Avandia] in ADOPT was associated with a higher risk of cardiovascular events, including heart failure, than glyburide."

G. The Bottom Falls Out on Avandia: 2007.

67. 2007 was a watershed year in the Avandia story. On May 21, 2007, the *NEJM* published the "Nissen" article, named after its lead author, Steven Nissen, M.D. This meta-analysis reviewed data compiled from 42 other studies and concluded that diabetic patients taking Avandia were ***43% more likely to suffer a heart attack*, and *64% more likely to die from cardiovascular causes than similar patients taking a different diabetes medication***. The authors obtained the raw data for their meta-analysis from a number of sources, including GSK's own website, the FDA, and online databases available to healthcare professionals. The authors

criticized GSK for failing to release a comprehensive set of data to allow independent researchers to conduct their own studies of Avandia. The authors observed:

> The manufacturer's public disclosure of summary results for rosiglitazone clinical trials is not sufficient to enable a robust assessment of cardiovascular risks. The manufacturer has all the source data for completed clinical trials and should make these data available to an external academic coordinating center for systematic analysis. . . . Further analyses of data available to . . . the manufacturer would enable a more robust assessment of the risks of this drug. Our data suggest a cardiovascular risk associated with the use of rosiglitazone.

In the same *NEJM* issue, two other prominent scientists stated in an editorial that, "[i]nsofar as the findings of Nissen . . . represent a valid estimate of the risk of cardiovascular events, rosigilitazone represents a major failure of the drug-use and drug-approval process in the United States." GSK had had all this data available at its fingertips for years, but it had at a minimum ignored the data, or at worst covered it up. Although GSK scientists had the ability and duty to analyze this data, GSK failed to take any action, all while aggressively marketing Avandia. Indeed, internal GSK e-mails show that GSK's own scientists ***confirmed*** the accuracy and validity of the Nissen analysis.

68. After the publication of the Nissen study, GSK went on the offensive. On June 5, 2007, in response to the Nissen study, GSK published "interim results" of its own RECORD (Rosiglitazone Evaluated for Cardiac Outcomes and Regulation of Glycaemia in Diabetes) study. It was no coincidence that GSK had these results prepared and ready for public dissemination only two weeks after the publication of the Nissen article. Unbeknownst to the Nissen article's authors, one of the medical doctors who was peer-reviewing the Nissen manuscript, Dr. Steven Haffner, had been paid over $75,000 in speaking and consulting fees by GSK. In a serious violation of the peer-review process, Dr. Haffner leaked the Nissen paper and its results to GSK weeks before its publication.

69. The RECORD study's stated purpose was to examine whether the "'promising' impact of thiazolidinediones on insulin sensitivity and cardiovascular risk factors would translate into an improvement in cardiovascular clinical outcomes."[5] The study also sought to "address concerns over cardiac failure[;] confirm that the better outcomes associated with improved glucose control, as reported by the UKPDS [the United Kingdom Prospective Diabetes Study], are applicable to this group of drugs; and allay concerns based on LDL [low-density lipoprotein] cholesterol concentrations rather than LDL particle atherogenicity." The publication of the RECORD study's interim results in June 2007 was the first that anyone in the United States, other than GSK, knew of the study's existence. In yet another violation of federal law, GSK failed to report this study's existence to the FDA. GSK released these "interim results" (the study had not been completed), to give a "complete picture" of Avandia's cardiovascular risks. RECORD's results showed that GSK's claims about Avandia's superior efficacy and safety were both false. The RECORD study confirmed that Avandia offered no superior efficacy over established diabetes drugs. And RECORD's "interim results" also showed that Avandia was associated with a 30% increased risk of heart failure. Minimizing and concealing the true results of its own RECORD study, GSK continued to claim that that the data were insufficient to support any conclusion about an increased risk of heart attacks.

70. The release of RECORD's "interim results" by GSK was calculated to prematurely publicize "conclusions" that were unsupported and, in fact, contradicted by the data from the study. Thus, for many scientists, RECORD raised more questions than it answered. As one researcher noted in an editorial in the *NEJM*, RECORD "seem[ed] to reflect a company-oriented posture regarding rosiglitazone, rather than a neutral scientific inquiry." Further, the

[5] This "purpose" is a startling admission that GSK's core marketing messages were false and misleading. Beginning in 1999, GSK was stating these "outcomes" as fact.

study had far too few participants, or "power," to extrapolate the study's findings beyond the study itself. But the study's primary weakness was that GSK lost track of nearly 10% of the study's participants after it began (called "loss-to-follow-up"), so the authors have no idea what happened to them.

71. Despite GSK's best efforts, it could not stem the tide of data exposing Avandia's dangers. On July 30, 2007, the FDA released its own meta-analysis of 42 studies. Like the Nissen study, the FDA's analysis drew largely on raw data of which GSK had known for years. And also like Nissen, the FDA's study found that Avandia significantly increased diabetics' risk of heart attacks and other serious cardiovascular events. The FDA's scientists found that Avandia use increased diabetics' already increased risk of serious cardiovascular events by ***an additional 42%***.

72. On the same day, the Endocrinologic and Metabolic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee of the FDA met jointly to examine the cardiovascular risks of Avandia. At that meeting, the FDA's Director for Science and Medicine in the Office of Surveillance and Epidemiology, Dr. David Graham, concluded that Avandia should be pulled from the market. His detailed presentation tracked a combination of results from long-term, placebo-controlled studies and meta-analyses to conclude that Avandia's benefits did not outweigh its cardiovascular risks.

73. After the close of testimony, the FDA Advisory Committee concluded that the use of Avandia for the treatment of Type 2 diabetes was associated with a greater risk of cardiovascular events, including heart attacks, than a placebo. Although the FDA's Advisory Committee found that the overall data was inconclusive as to the association of Avandia to cardiovascular events as compared to other anti-diabetic drugs, such as metformin or

sulfonylureas, after further discussion with other FDA committees and experts, the FDA nonetheless concluded that a black-box warning of such risks was necessary.

74. On September 23, 2007, a third independent meta-analysis was published, this time by the Journal of the American Medical Association ("*JAMA*"). This analysis confirmed both the Nissen and the FDA's results, showing a 42% increase in heart attacks associated with Avandia use. The *JAMA* study concluded that Avandia "significantly increased the risk of myocardial infarction." Also in September 2007, a study published in the *Annals of Internal Medicine* concluded that, compared "with newer, more expensive agents [like Avandia], older agents (second-generation sulfonylureas and metformin) have similar or superior effects on glycemic control, lipids, and other intermediate endpoints."

75. Finally, on November 14, 2007, the FDA mandated that GSK add a warning to the Avandia label listing heart attacks as a potential side effect. More specifically, the additional warning information reads in part:

> A meta-analysis of 42 clinical studies (mean duration 6 months; 14,237 total patients), most of which compared AVANDIA to placebo, showed AVANDIA to be associated with an increased risk of myocardial ischemic events such as angina or myocardial infarction.

76. Spurred by these events, the United States Senate Finance Committee launched an investigation into GSK and its handling of Avandia. The Committee released its report, *The Intimidation of Dr. John Buse and the Diabetes Drug Avandia*, in November 2007. The Committee found that "executives at the highest levels of GSK" were involved in an organized attempt to intimidate Dr. Buse into silence. The Committee found that "GSK executives labeled Dr. Buse a 'renegade' and silenced his concerns about Avandia by complaining to his superiors and threatening [him with] a lawsuit." After reviewing GSK's internal documents and correspondence regarding Dr. Buse, the Senate Committee concluded that "it is apparent that the

original allegations, regarding Dr. Buse and GSK's attempts at silencing him are true. Even more troubling, documents reveal that plans to silence Dr. Buse involved discussions by executives at the highest levels of GSK, including then and current CEO Jean-Pierre Garnier."

77. The Senate Finance Committee report chastised GSK for placing its interests above the public well-being. The Committee report found:

> Corporate intimidation, the silencing of scientific dissent, and the suppression of scientific views threaten both the public well-being and the financial health of the federal government, which pays for health care. The behavior of GSK during the time that Dr. Buse voiced concerns regarding the cardiovascular risks he believed were associated with Avandia was less than stellar. Had Dr. Buse been able to continue voicing his concerns, without being characterized as a "renegade" and without the need to sign a "retraction letter," it appears that the public good would have been better served.

78. Despite the overwhelming evidence establishing otherwise, GSK continued to deny evidence of the increased cardiovascular risks associated with Avandia. In December 2007, in response to the *JAMA* meta-analysis, GSK baldly stated in a press release that "there is no consistent or systematic evidence that [Avandia] increases the risk of myocardial ischemic events or deaths in comparison to other anti-diabetic agents."

H. The Impact of GSK's False and Deceptive Marketing of Avandia.

79. While Avandia remains on the market, its days appear to be numbered. Indeed, since its peak in 2007, Avandia sales have declined 70%. Further, numerous healthcare providers like Prime Therapeutics and Health Transmark have dropped Avandia from their approved drugs lists because of Avandia's safety concerns. The Veteran's Administration, the American Diabetes Association, the ADA's European counterpart, Kaiser Permanente, and the COUNTY OF SANTA CLARA have all followed suit. Clearly, had the truth about Avandia's increased cardiovascular risk that was known by GSK been made available to California diabetics, their insurers, public health care providers, public entities, and government payors,

including Plaintiff COUNTY OF SANTA CLARA, millions of Avandia prescriptions would never have been written.

80. While more studies have been published since 2007 that, cumulatively, reveal the scope of Avandia's dangers, a study that may close the book on the Avandia story was released in February 2010. Published in the journal for the American Diabetes Association, *Diabetes Care*, the recent study sought to "identify potential association(s) of diabetic medications with myocardial infarction (MI)." As GSK purported to do in the ADOPT and RECORD studies, researchers at Harvard University compared Avandia to the established and much cheaper drugs metformin and sulfonylureas. They also included another TZD, pioglitazone (also known as Actos). The study reviewed the charts for groups of 11,200, 12,490, 1,879, and 806 patients who were prescribed sulfonylurea, metformin, Avandia, or Actos, respectively. The Harvard study found that, compared to sulfonylurea, Avandia increased a diabetic's heart attack risk by an additional 30%. Significantly, when contrasted with GSK's claims to the contrary, the Harvard study showed that when compared to metformin, the "gold standard" in diabetes treatment, Avandia more than doubled a diabetic's risk of heart attack, increasing the risk by 120%. This led the authors dryly to conclude that "[o]ur results are consistent with a relative adverse cardiovascular risk profile for rosiglitazone." This is hardly the "significant advance" in diabetes care that GSK represented Avandia would be beginning in 1999 and continuing thereafter.

81. As discussed above, GSK spent hundreds of millions of dollars to launch and maintain a massive promotional campaign to drive Avandia's sales. Avandia's blockbuster sales figures were driven by GSK's decision to put marketing, sales, and corporate profits ahead of science and patient safety. GSK knew that the dissemination of information about Avandia's true cardiovascular risks would devastate its sales and make Avandia unable to compete with

other established—and safer—diabetes therapies. Thus, GSK intentionally chose – and continues to choose – to put its corporate profits ahead of patient safety and repeatedly failed – and continues to fail – to disclose critical safety information, information that has led to a black box warning, resulted in removal from formularies, and that likely will mean ultimately that Avandia is removed from the market.

82. Had GSK refrained from engaging in misleading and deceptive promotion of the drug, and instead been forthcoming and disclosed the true facts about Avandia, sales of the drug would have been a small fraction of the billions that GSK made over the years, ***if any at all***. In recent and separately authored reports, prominent FDA scientists Drs. Kate Gelperin and David Graham each recommend Avandia be pulled from the market entirely. GSK's misleading and deceptive marketing of Avandia continues today, with a vigorous defense of Avandia's purported safety and efficacy and heavy reliance on anticipated results of an ongoing clinical trial that, on information and belief, is being conducted without sufficient independent scientific oversight or access by the scientific community to the underlying data.

83. As shown above, GSK's corporate strategy and business model is dictated not by science, but by sales and marketing. At GSK, marketing and commercial personnel exert extensive control over scientific and medical decisions, such as the initiation of clinical trials, the types of trials done, the design of those trials, and the reporting and publication of the data, all with the ultimate goal of producing further support for GSK's marketing messages and bolstering sales of Avandia. For example, on information and belief, GSK actively sought to create the impression that Avandia was better at lowering blood sugar than metformin, but intentionally avoided studying these two drugs head-to-head because it knew that if it did so, the studies would show GSK's claims to be false. GSK also obscured or failed to report important

safety information specifically relating to Avandia's cardiovascular risk, because doing so would jeopardize sales of Avandia and would be inconsistent with GSK's key marketing and sales messages—such as GSK's claim that Avandia, even though more expensive, ultimately was more cost effective than other type 2 diabetes therapies. GSK's top priority is neither science nor safety, but rather marketing. Marketing concerns infected and distorted GSK's entire Avandia scientific program and continue to do so to this day.

84. Likewise, GSK maintained a marketing-based publication strategy to misleadingly influence the medical and scientific literature by promoting the publication of medical and scientific articles that would support its marketing message about Avandia's safety and efficacy and/or suggest dissatisfaction with competing therapies. On information and belief, this strategy included practices such as ghostwriting articles and hiring outside ghostwriting companies, giving GSK's marketing personnel editorial and substantive input into decisions about what scientific studies to publish and the actual content of such publications, and forming misleading financial and promotional relationships with authors, "opinion leaders" and other physicians. GSK gave its marketing department extensive control over the company's research and publication decisions so that medical and scientific publications could be used as tools to promote its marketing messages about Avandia.

85. Further, marketing studies have shown that as the truth about Avandia became known, most former California diabetics, their insurers, public health care providers, public entities, and government payors, including Plaintiff COUNTY OF SANTA CLARA, returned to the established diabetes medicines like metformin and sulfonylureas. And as the truth about Avandia has continued to come out, despite GSK's continuing efforts to suppress and mislead, Avandia's sales have continued and will continue to drop. In the meantime, however, GSK is

continuing its practice of misleading and deceptive marketing of Avandia, is continuing to conduct a clinical trial behind closed doors to prevent independent scientific analysis of the raw data, and is continuing to reap profits from sales of Avandia.

86. In short, GSK bilked purchasers, including California diabetics, their insurers, public health care providers, public entities, and government payors, including Plaintiff COUNTY OF SANTA CLARA, out of hundreds of millions of dollars by making false representations that Avandia was better at lowering blood sugar and could decrease diabetics' cardiovascular risks. Plaintiff COUNTY OF SANTA CLARA alone paid approximately $2 million for Avandia between May 1999 and July 2009, with a sharp drop in purchases beginning in mid-2007, when the County advised all prescribing physicians of the FDA's 2007 warning letter regarding Avandia's risks and suggested that physicians "may choose to take a pro-active approach and contact [their] patients directly to discuss the risks and benefits of remaining on Avandia versus changing therapy." In September 2009, the County removed Avandia from its formulary. Moreover, from the time it first went on the market, Avandia's price was grossly inflated compared to older diabetes drugs. In October 2007, the average monthly prescription cost for older agents like metformin and the sulfonylurea glipizide ranged from $4 to $100. The cost for Avandia was from $90 to $220.

87. But the greatest cost of GSK's failure to warn and its false and deceptive advertising was to the population of people, recognized as disabled under California law, whom GSK specifically targeted for its false and deceptive marketing: diabetics. Because of the disease itself, this population was already at an increased risk for cardiovascular problems, including heart attacks. As Dr. Graham noted at the FDA Advisory Committee meeting on July

30, 2007, from Avandia's launch in 1999 through 2006, Avandia likely caused between 60,000 and 200,000 excess heart attacks, strokes, and other cardiovascular deaths.

I. GSK's Fraudulent Concealment.

88. GSK employed practices and techniques of secrecy in order to avoid detection of, and fraudulently to conceal, its deceptive and conspiratorial behavior regarding the true lack of safety and efficacy of Avandia and Avandia's concomitant increased cardiovascular risks. Defendants successfully concealed from the scientific community and the general public facts sufficient to arouse suspicion of the existence of the claims that Plaintiffs COUNTY OF SANTA CLARA and the PEOPLE were not alerted to the existence and scope of this industry-wide fraud and could not have acquired such knowledge earlier through the exercise of reasonable diligence. Through its public statements, marketing, and advertising, GSK's self-concealing scheme and affirmative conduct to perpetuate this fraud deprived California diabetics, their insurers, public health care providers, public entities, government payors, including Plaintiff COUNTY OF SANTA CLARA, and the PEOPLE of actual or presumptive knowledge of facts sufficient to put them on notice of potential claims.

89. On November 15, 2012, the People of the State of California, acting by and through the Attorney General for the State of California, the Honorable Kamala D. Harris ("CA Attorney General"), filed a lawsuit against GSK in the Superior Court of the State of California for the County of San Diego, Case No. 37-2012-00085491-CU-MC-CTL (the "California AG Action"). The California AG Action alleged violations of California's Unfair Competition Law located at California Business and Professions Code section 17200 et seq. and California's False Advertising Law located at California Business and Professions Code section 17500 et seq. concerning GSK's marketing and sales of Avandia in California.

90. Also, on or about November 15, 2012, GSK and the CA Attorney General entered into a stipulated judgment resolving certain of the claims alleged by the People of the State of California in the California AG Action. That judgment was filed with and entered by the Court

on November 15, 2012. In addition to setting forth the nature and scope of the settlement between GSK and the CA Attorney General resolving the California AG Action, the judgment also provided, at paragraph 11, that certain claims of certain persons were not released and not affected by the judgment. In this regard, as pertinent here, the judgment provides in pertinent part as follows:

> 11. Notwithstanding any term of this Judgment, specifically reserved and excluded from the Released Claims as to any entity or person, including Released Parties, are any and all of the following:
>
> ...
>
> C. Actions of state program payors of the State of California arising from the Covered Conduct, except for the release of civil penalties under the State of California's above-cited state consumer protection law.
>
> D. Any claims individual consumers have or may have under the State of California's consumer protection laws against any person or entity, including Released Parties.
>
> E. Any claims that have been brought by the Santa Clara County Counsel's Office, as of the date of entry of this Judgment, for violations of California Business and Professions Code section 17500 concerning all Covered Conduct as defined in this Judgment, to which persons resident in the County of Santa Clara were exposed. This exclusion applies to and in favor of only persons or entities resident in the County.

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FIRST CAUSE OF ACTION

Violations of California Business and Professions Code Section 17500, *et seq.*,

by Plaintiffs COUNTY OF SANTA CLARA and THE PEOPLE OF THE STATE OF CALIFORNIA, acting by and through Acting Santa Clara County Counsel Lori E. Pegg (False Advertising)

91. Plaintiffs incorporate and re-allege Paragraphs 1 through 90 as though fully set forth herein.

92. From May 25, 1999 through the present, GSK, directly or indirectly, violated California Business and Professions Code section 17500 by making or disseminating untrue, false, or misleading statements about Avandia, or causing untrue, false, or misleading statements about Avandia to be made or disseminated to the general public. Further, GSK continually and repeatedly failed to disclose material facts. Such omissions, while false, deceptive, and misleading in their own right, also made seemingly truthful statements false, deceptive, and misleading. All of this conduct, separately and collectively, was likely to deceive California diabetics, their insurers, public health care providers, public entities, and government payors, including Plaintiff COUNTY OF SANTA CLARA.

93. GSK engaged in a widespread promotional campaign including supporting direct- to-consumer advertising, marketing to physicians, marketing to payors, influencing the medical and scientific literature, employing sales representatives and speakers, public relations and other efforts to drive the sales of Avandia by creating a false and misleading impression of the limited benefits and significant cardiovascular risks of the product. GSK also failed to disclose the true risks in its product labeling, communications and promotional materials and, in particular, failed to disclose significant cardiovascular risks about which it knew or should have known.

94. In addition, GSK represented that Avandia was a safe and effective drug when it knew or should have known that these representations were untrue, false, or misleading; it represented that Avandia was a safer and more effective drug than its competitors when it knew or should have known that those representations were untrue, false, or misleading; it represented that Avandia was a "significant advance" in the treatment of diabetes when it knew or should have known that the representation was untrue, false, or misleading; and it represented that Avandia could decrease the cardiovascular risks attendant to diabetes (or at least that it would not increase those risks) when it knew or should have known that those representations were untrue, false, or misleading. GSK concealed and failed to disclose to California diabetics, their insurers, public health care providers, public entities, government payors, including Plaintiff COUNTY OF SANTA CLARA, and the PEOPLE data and scientific studies it conducted showing Avandia could cause serious cardiovascular events. GSK failed to disclose to California diabetics, their insurers, public health care providers, public entities, government payors, including Plaintiff COUNTY OF SANTA CLARA, and the PEOPLE scores of adverse event reports linking Avandia to serious cardiovascular events. GSK failed to disclose to doctors, diabetics, purchasers including Plaintiff COUNTY OF SANTA CLARA, and the PEOPLE the existence of numerous scientific studies showing Avandia was no better than competitor drugs at lowering blood sugar.

95. GSK knew, or by the exercise of reasonable care should have known, at the time of making these statements, or causing these statements to be made, that such statements were false, untrue, or misleading and therefore, likely to deceive the public. In addition, GSK knew or should have known that its marketing and promotional efforts were creating a false and misleading impression of the risks of the product.

96. One of the remedies available under California Business and Professions Code

Section 17535, in addition to the restitution and civil penalties sought above, is the issuance of injunctive relief. As described above, GSK engaged in numerous false, misleading and/or deceptive acts and omissions in connection with marketing and promoting Avandia, beginning even before Avandia was placed on the market and continuing throughout the years. GSK continues to engage in such conduct with respect to the drug Avandia, as well as on a companywide basis.

97. On information and belief, GSK's clinical research and publication strategies are directed and influenced largely by marketing concerns rather than by medical or safety concerns, and GSK's management allows marketing personnel to direct the company's so-called scientific research rather than enabling independent analysis. GSK repeatedly failed to disclose important safety information; it improperly and deceptively influenced the medical and scientific literature and the perception of Avandia within the medical community; it consistently downplayed Avandia's risks; it formed deceptive and misleading financial and promotional relationships with "opinion leaders," speakers and other physicians for the purpose of promoting the product; it engaged in misleading sales training, sales tactics, and marketing to physicians that misrepresented the safety and efficacy of Avandia; it engaged in the ghostwriting of medical and scientific articles; and it engaged in other deceptive and misleading marketing, lobbying, public relations, and sales practices. On information and belief, this pattern of conduct continues to this day in an apparent attempt to avoid decreased sales and/or an FDA ban. GSK's marketing of Avandia continues to drive research decisions, including by restricting the availability of factual information so as to prevent independent scientists from analyzing the data and confirming Avandia's serious dangers.

98. Further, on information and belief, the nature of GSK's conduct with respect to Avandia is simply an extension of companywide methods and practices regarding the

promotion, marketing, and sale of GSK's pharmaceutical products throughout the State of California and throughout the United States. Not only is such conduct ongoing, it is likely to continue to occur without the issuance of injunctive relief against GSK.

99. To prevent GSK's ongoing and future misleading and deceptive sales, marketing, and promotional conduct with respect to Avandia, including that which is done under the guise of research, publication, and educating individuals or physicians, Plaintiffs COUNTY OF SANTA CLARA and the PEOPLE seek injunctive relief (a) prohibiting all GSK employees previously or currently engaged in marketing, sales, physician education, or product placement from directing, advising, or otherwise influencing decisions regarding scientific, medical, or clinical research, analysis or disclosure, including with respect to the initiation of and methods of conducting clinical trials, the types of trials done, the design of those trials, the reporting and publication of data from those trials, the publication of medical or scientific literature, and the dissemination of safety information; and (b) enjoining GSK's existing scientific data publication policy, and requiring GSK to fully and publicly disclose all of the source data for completed and ongoing clinical trials and to make these data available to an external academic coordinating center for systematic analysis.

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PRAYER FOR RELIEF

WHEREFORE, Plaintiffs COUNTY OF SANTA CLARA and THE PEOPLE OF THE STATE OF CALIFORNIA, acting by and through Acting Santa Clara County Counsel Lori E. Pegg, pray for relief against Defendants, and each of them, to the extent permitted by Paragraph 11(E) of a Final Judgment entered in *People of the State of California v. GlaxoSmithKline LLC* on November 15, 2012, as follows:

I. Pursuant to California *Business and Professions Code* section 17535, restitution of any money acquired by Defendants' violations of California *Business and Professions Code* section 17500;

II. Pursuant to California *Business and Professions Code* section 17536, an order assessing a civil penalty of two thousand five hundred dollars ($2,500) against Defendants for each violation of California *Business and Professions Code* section 17500, defined as each prescription for Avandia issued in the County of Santa Clara, California from May 25, 1999 through the present;

III. Pursuant to California *Civil Code* section 3345, an order trebling all relief awarded by the Court;

IV. Pursuant to California *Business and Professions Code* 17535, permanent injunctive relief against Defendants;

V. Prejudgment interest at the maximum legal rate;

VI. Costs of the proceedings herein;

VII. Reasonable attorneys' fees and costs; and,

VIII. Such other and further relief remaining or existing under paragraph 11 of the California Superior Court's Final Judgment.

Dated: February 22, 2013

Respectfully submitted,

By: 

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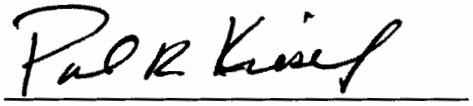
Attorneys for Plaintiffs COUNTY OF SANTA CLARA and THE PEOPLE OF THE STATE OF CALIFORNIA

DEMAND FOR JURY TRIAL

Plaintiffs COUNTY OF SANTA CLARA and THE PEOPLE OF THE STATE OF CALIFORNIA hereby demand a trial by jury.

Dated: February 22, 2013

Respectfully submitted,

By: 

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CERTIFICATE OF SERVICE

I hereby certify that, on February 22, 2013, I caused the foregoing STIPULATION PURSUANT TO FED. R. CIV. P. 15(A)(2) FOR PLAINTIFF TO FILE A SECOND AMENDED COMPLAINT to be served, via email and first-class mail, on:

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